IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:	Confirmation No.: 1226
Bamdad *et al.*	Examiner: LU, Frank Wei Min
Application No.: 10/016,416	Art Unit: 1634
Filed: December 10, 2001	*Certificate of Transmission (37 C.F.R. § 1.8)*
For: Detection of Target Analytes Using Particles and Electrodes	*I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system in accordance with § 1.6(a)(4) on* 3/13/2009
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APPELLANTS' BRIEF UNDER 37 C.F.R. § 41.37

This Brief is filed in support of Appellants' appeal from the Examiner's Rejection dated May 28, 2008. No claims have been allowed and claims 18, 20-27 are pending. Claims 18, 20-25, and 27 are appealed. A Notice of Appeal and Pre-Appeal Conference Request were filed on September 2, 2008. A decision of the Pre-Appeal Conference that affirms the Examiner's rejections was mailed on November 18, 2008. As such, this Appeal Brief is timely filed.

The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134.

The Commissioner is hereby authorized to charge deposit account number 50-0310, order no. 067456-5020-US01 to cover the fee required under 37 C.F.R. §1.17(c) for filing Appellants' brief. In the unlikely event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, Appellants petition for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit account number 50-0310, order no. 067456-5020-US01.

1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit account number 50-0310, order no. 067456-5020-US01.

TABLE OF CONTENTS

TABLE OF CONTENTS
(continued)

Page

REAL PARTY IN INTEREST

The real party in interest in this appeal is Osmetech Technology Inc., the assignee of this application.

RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any related appeals or interferences which will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

STATUS OF THE CLAIMS

The present application was filed on December 10, 2001 with claims 1-17. During the course of prosecution, claims 18-37 were added, claims 1-17, 19, and 28-37 were canceled, claim 26 was withdrawn. Accordingly, claims 18, 20- 25, and 27 are pending and stand rejected in the present application and are appealed herein.

STATUS OF AMENDMENTS

All amendments have been entered. A copy of the rejected claims is attached as Claims Appendix.

SUMMARY OF THE CLAIMED SUBJECT MATTER

Below is a description of each appealed claim and where support for each can be found in the specification.

Independent claim 18 claims a composition. The composition comprises: (a) a substrate comprising an array of working electrodes, wherein each electrode comprises a first binding ligand; (b) a plurality of colloids, each comprising: (i) a second binding ligand; and (ii) an electron transfer moiety; and (c) a detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety (see original claims 1-6 and specification in FIGs. 1-3, page 2, line 36 to page 3, line 5, page 3, line 14 to page 4, line 7, page 11, lines 10 and 35, page 70, lines 18-25, and page 74, lines 16-25).

Claim 20 depends from claim 18 wherein the plurality of colloids further comprise a self-assembled monolayer (see original claims 1 and 2 and specification in page 46, lines 28-30).

Claim 21 depends from claim 20 wherein the self-assembling monolayer comprises an alkyl chain (see specification in page 25, line 32).

Claim 22 depends from claim 18 wherein the substrate is a printed circuit board (see specification in page 11, line 36 to page 12, line 2).

Claim 23 depends from claim 18 wherein the electrodes are gold (see specification in page 11, line 15).

Claim 24 depends from claim 18 wherein the electron transfer moiety is a transition metal complex (see specification in page 50, line 36).

Claim 25 depends from claim 24 wherein the transition metal complex is ferrocene (see specification in page 52, line 13).

Claim 27 depends from claim 18 wherein the first binding ligand is a first nucleic acid and the second binding ligand is a second nucleic acid (see specification in page 3, line 4 to page 4, line 7).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

As addressed individually below, Appellants request review of the Examiner's final rejections of: (1) claims 18, 20, 24 and 27 under 35 U.S.C. § 103(a) over Sigal et al. (U.S. Patent No. 6,319,670 B1) ("*Sigal*") in view of Meade et al. (U.S. Patent No. 5,770,369) ("*Meade*") and Roberts et al. (U.S. Patent No. 5,958,791) ("*Roberts*"), (2) claim 21 under 35 U.S.C. § 103(a) over *Sigal* in view of *Meade* and *Roberts*, and further in view of Bamdad et al. (U.S. Patent No. 5,620,850) ("*Bamdad*"), (3) claim 22 under 35 U.S.C. § 103 over *Sigal* in view of *Meade* and *Roberts*, and further in view of Gerpheide et al. (U.S. Patent No. 5,565,658) ("*Gerpheide*"); (4) claim 23 under 35 U.S.C. 103(a) over *Sigal* in view of *Meade* and *Roberts*, and further in view of Kayyem et al. (U.S. Patent No. 6,096,273) ("*Kayyem*"); (5) claim 25 under 35 U.S.C. 103(a) over *Sigal*, in view of *Meade* and *Roberts*, and further in view of *Kayyem*; (6) claim 23 under 35 U.S.C. 103(a) over *Sigal* in view of *Meade* and *Roberts*; and (7) claim 25 over *Sigal* in view of *Meade* and *Roberts*.

ARGUMENTS

Appellants submit that the 35 U.S.C. § 103(a) rejection cannot be sustained for numerous reasons. First of all, the references in combination do not teach "an array of working electrodes."[1] Secondly, there is no motivation to combine *Sigal* with *Meade* or *Roberts* because

[1] With the exception of *Kayyem*, which as shown below is improperly cited as prior art.

the proposed modification would change the principle of operation of *Sigal*, render the assays of *Sigal* unsatisfactory for their intended purpose, and there is no reasonable expectation of success by combining *Sigal* with *Meade*. Thirdly, *Gerpheide* explicitly teaches away from *Roberts*. Finally, the Examiner erred in citing *Kayyem* which cannot preclude patentability of the presently claimed invention under 35 U.S.C. § 103.

Each of these points is addressed below.

I. The Rejection of Claims 18, 20, 24 and 27 Under 35 U.S.C. § 103(a) Over *Sigal* In View of *Meade* and *Roberts* Are Improper Because the References In Combination Do Not Teach "An Array of Working Electrodes" And There Is No Motivation to Combine *Sigal* With *Meade* Or *Roberts*

Claims 18, 20, 24 and 27 stand rejected under 35 U.S.C. § 103(a) over *Sigal* in view of *Meade* and *Roberts*.

When rejecting claims under 35 U.S.C. §103, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. MPEP § 2142. The inquiry of obviousness is controlled by the *Graham* factors. See *KSR International Co. v. Teleflex Inc.* 1727 S.C.t (2007) (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966)). These factors are: 1) the scope and content of the prior art; 2) the differences between the prior art and the claims; 3) the level of ordinary skill in the pertinent art; and 4) objective evidence of nonobviousness.

A. Description of the Prior Art

1). *Sigal*

Sigal is directed to compositions and methods used to measure the presence of analyte by measuring electrochemiluminescence triggered by a voltage imposed on a working electrode. *See* col. 1, ll. 15 – 19 and ll. 48-49. In electrochemiluminescence assays, a reactive species is reduced and thus placed in an excited state. Upon relaxation, a photon is emitted and detected by a photomultiplier tube (PMT). *See* col. 17, ll. 25-28.

On page 3 of the final Office Action mailed on May 28, 2008 ("Office Action") the Examiner concedes that "Sigal et al. do not disclose a substrate comprising an array of electrodes

and a detector capable of detecting the voltage associated with electron transfer moiety." (Emphasis added).

2). *Meade*

Meade is directed to electron transfer via nucleic acids. *See* col. 1 ll. 11-12. The Examiner relies on *Meade* to provide the motivation for replacing the photon detector of *Sigal* with the "detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety" as recited in the claims. *See* pages 4-5 of the Office Action.

3). *Roberts*

Roberts is directed to a test device for detecting or determining an analyte in a test solution. *See* Abstract. The test device

> includes an absorbent material, having a contact portion proximate to one end for contact with and uptake of the test solution. Positioned away from the first end of the absorbent material, there is an electrochemical measurement portion having a first conductor and a second conductor. Each conductor comprises a plurality of fingers disposed on the absorbent material, and the fingers of the first conductor are interdigitated with the fingers of the second conductor. (Emphasis added) Col. 5, ll. 33-43.

Roberts further states in col. 8, ll. 18-30 that:

> Advantages of fabricating small electrodes in interdigitated arrays go even further by allowing redox cycling of ions back and forth between anode(s) and cathode(s)..... By using a dual potentiostat and a four-electrode system with an interdigitated array, it is possible to almost completely eliminate charging current (emphasis added).

FIG. 1 of *Roberts* shows an embodiment with four conductors (electrodes): first conductors **130** and **134** and second conductors **132** and **136**. "Each conductor (or electrode) comprises a plurality of fingers disposes on the absorbent material, and interdigitated with the fingers of the other conductor (emphasis added)." *See* col. 9, ll. 9-10. Two pairs of the conductors are separately located in two different channels: **130** and **132** in the control channel D, and **134** and **136** in the control channel E. *See* FIG. 1 and col. 15, ll. 17-32. FIG. 2a shows the enlarged view of "an interdigitated electrode array as shown in FIG. 1." Col. 8, ll. 44-46.

Therefore, *Roberts* teaches a pair of electrodes: one working electrode having multiple fingers interdigitated with one reference electrode that also having multiple fingers. Thus, *Roberts* does not teach "an array of working electrodes" or electrodes that form an array. Instead, *Roberts* teaches two electrodes, each comprises an array of fingers, ("with an interdigitated array") and the fingers are only part of the electrode.

B. The References in Combination Do Not Teach "An Array of Working Electrodes."

Claims 20-25 and 27 depends from claim 18 which recites "an array of working electrodes."

The Examiner concedes *Sigal* does not teach "an array of electrodes." *See* page 3 of the Office Action. Nevertheless, the Examiner states that "the rejection ... is based on the combination of patents ... Roberts et al. teach the motivation to form an array of working electrode[s]." See page 7 of the Office Action. Appellants respectfully disagree.

M.P.E.P. § 21.41III states:

> The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art.... The gap between the prior art and the claimed invention may not be "so great as to render the [claim] nonobvious to one reasonably skilled in the art." (Citation omitted).

As presented above, *Roberts* does not teach "an array of working electrodes" or electrodes that form an array. Instead, *Roberts* teaches two electrodes, each comprises an array of fingers, and the fingers are only part a single working electrode system.

The Examiner also cites *Roberts* for its disclosure of the "advantage of fabricating small electrode in interdigitated arrays." Page 4 of Office Action. The Examiner further alleges that:

> Roberts *et al.* suggest that advantage of fabricating small electrodes in interdigitated arrays "[M]icroelectrodes fabricated in an interdigitated array have inherent advantages in signal detection over more conventional electrode configurations... Scaling down the size of an individual electrode has the advantage of increasing the rate of mass transport, increasing the signal-to-noise (faradaic/charging current) ratio, and decreasing ohmic signal loss... Advantages of fabricating small electrodes in interdigitated array go even further by allowing redox cycling of ions back and forth between anode(s) and cathode(s)... This

> generates much larger current for detection and allows for the use of extremely small sample volumes" (see column 8), Roberts *et al.*, teach the motivation to form an array of working electrode recite in claim 18. Office Action, at page 7.

However, *Roberts* only discloses "small electrodes" and the additional advantage of "fabricating small electrodes in interdigitated arrays." The "array" of *Roberts* refers to is an array of "fingers" of each electrode; it does NOT refer to an array of electrodes, nowhere does *Roberts* disclose an array of electrodes. The advantages of "increasing the size of mass transport, increasing the signal-to-noise (faradaic/charging current) ratio, and decreasing ohmic signal losses" are in reference to the small scale of the *Roberts* electrodes, rather than to any configuration of working electrodes. Therefore, and contrary to the Examiner's assertion, *Roberts* does not teach the motivation for forming an array of working electrodes.

Because *Roberts* does not teach, or teach the motivation to form, "an array of electrodes," the references in combination do not teach "an array of working electrodes" as the pending claims require. As such, the gap between the combination of *Sigal, Meade*, and *Roberts* and the claimed invention is so great as to render the pending claims nonobviousness to one reasonably skilled in the art. Accordingly, the Examiner failed to establish a *prima facie* case of obviousness.

C. There Is No Motivation to Combine *Sigal* with *Meade* or *Roberts*

The Examiner concedes *Sigal* does not teach "an array of electrodes." See page 3 of Office Action. Nevertheless, the Examiner states that "the rejection is not based on only one patent from Sigal et l., Meade et al., and Roberts et al., but is based on the combination of patents from Sigal et l., Meade et al., and Roberts et al." See page 7 of Office Action. Appellants respectfully disagree.

M.P.E.P. § 2143.01.III states:

> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007).

"[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does." *KSR*, at 1741. Appellants contend that there is no motivation to combine the references.

First of all, as presented above, the advantages of "increasing the size of mass transport, increasing the signal-to-noise (faradaic/charging current) ratio, and decreasing ohmic signal losses" are in reference to the small scale of the *Roberts* electrodes, rather than to any configuration of working arrays.

Secondly, as presented in more detail below, the principle of operation of *Sigal* is different from that of the claimed invention. *Sigal* depends on the detection of photons; the pending claims are directed to detection of a voltage. The combination of *Sigal, Meade*, and *Roberts* would change the principle of operation of *Sigal*, rendering compositions and methods for conducting electrochemiluminescence binding assays of *Sigal* unsatisfactory for their intended purpose.

Finally, as outlined below, there is no a reasonable expectation of success by combining *Sigal* in view of *Meade*.

1). The proposed modification or combination of *Sigal* with other references would change the principle of operation of *Sigal.*

The Examiner concedes that "Sigal *et al.* do not disclose a substrate comprising an array of electrodes and a detector capable of detecting the voltage associated with electron transfer moiety as recited in a) and c) of claim 18." Page 3 of the Office Action. The Examiner relies on *Meade* to provide the motivation for replacing the photon detector of *Sigal* with the "detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety" as recited in the claims. See page 8 of the Office Action. However, because the proposed modification of will change the principle of *Sigal*, there is no motivation for a skilled artisan to make such modification. M.P.E.P. § 2143.02 VI states:

> If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

The present invention is directed to the detection of electrons (detecting transfer using "a detector that is capable of detecting a voltage"), which is different from *Sigal* that teaches the detection of photons (electrochemiluminescence).

Sigal is directed to compositions and methods used to measure the presence of analyte by measuring electrochemiluminescence triggered by a voltage imposed on a working electrode. See col. 1, lines 15 – 19 and lines 48-49. In electrochemiluminescence assays, a reactive species is reduced and thus placed in an excited state. Upon relaxation, a photon is emitted and detected by a photomultiplier tube (PMT). This is in contrast to electron transfer, which is detected using a detector that is capable of detecting voltage rather that photons.

The Examiner fails to distinguish between detection of photons (electrochemiluminescence) and detection of electrons (electron transfer). The Examiner states in pages 8 -9 of the Office Action:

> [T]he detector capable of detecting the integrated photocurrent associated with electron transfer from said ECL comprising electron transfer moiety taught by *Sigal et al.*, and the detector capable of detecting the voltage associated with electron transfer taught by Meade et al., are used for the same purpose (ie., detecting electron transfer of the transitional metal complex), the detector taught by Sigal *et al.*, and the detector taught by Meade et al., are exchangeable in order to detect electron transfer of the transitional metal complex.

Thus, the Examiner assumes that the principle of operation of *Sigal* is "to detect electron transfer of the transitional metal complex." Appellants respectfully disagree.

Reviewing *Sigal* immediately shows that *Sigal* is specifically and solely directed to electrochemiluminescence that is based on the detection of photons, rather than electrons. For example, the Title of *Sigal* is "Methods and Apparatus for Improved Luminescence Assays Using Micropaticles." In the section tiled "Filed of the Invention" *Sigal* states: "This application relates generally to methods and compositions for conducting binding assays, more particularly to those which measure the presence of an analyte of interest by measuring electrochemiluminescence emitted by one or more labeled components of the assay system." (Emphasis added.) Col. 1, ll. 15-19. In the section titled "Objects of the Invention" *Sigal* further states: "a primary object of this invention to provide methods, reagents and compositions, for conducting of electrochemiluminescence binding assays." (Emphasis added). Col. 2, ll. 12-23. In the section titled "Summary of the Invention" *Sigal* states that:

> These and other objects of the invention are achieved using microparticles comprised of an electrically conductive material having (a) one or more copies of an assay ligand immobilized on its outer surface, and (b) a plurality of ***electrochemiluminescent moieties*** immobilized on its outer surface. The assay ligand may be linked to the ***electrochemiluminescent moiety***. More specifically, it

> has now been found that colloidal gold is a highly advantageous conductive material with which to form microparticles. Colloidal gold particles having one or more assay ligands immobilized on its outer surface and a plurality of ***ECL moieties*** immobilized on its outer surface can be used in a wide range of assay formats, including those based on ***detecting the ECL*** from moieties immobilized on the particle and those based on the modulation by the particles of the ***ECL from free ECL moieties in*** solution. The objects of the present invention may also be achieved using microparticles that do not comprise electrically conductive material. (Emphasis added.) Col. 2, ll. 46-64.

As such, in *Sigal*, although the photons are detected by detecting electrons, those electrons are produced due to photoelectric effect (the generation of electrons when photons strike a photocathode material in the PMT), not due to electron transfer. These two concepts are quite different. Adding the detector of *Meade* to *Sigal* would result in no signal – the assay would be inoperable, and in fact, changing the operability of *Sigal*, thus "change the principle of operation." The same is true of the reverse situation.

As clearly stated by M.P.E.P. § 2143.02 VI and cases including *In re Ratti*, the inoperability of the combination is a strong factor that requires a finding a non-obviousness. Because the combination would change the principle of operation of *Sigal*, there is no reason to prompt a skilled artisan in the relevant field to combine *Sigal* with other references in the way the claimed invention does.

2). The proposed modification of *Sigal* in view of *Meade* would render the assays of *Sigal* unsatisfactory for their intended purpose.

M.P.E.P §2143.01V also states:

> If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)

Claim 18 recites "a detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety." Thus, the detector of claim 18 does not detect photons. Therefore, the ligand binding according to *Sigal* could not be detected. Accordingly, the compositions and methods for conducting electrochemiluminescence binding assays of *Sigal* would not achieve their intended purpose if the detector of claim 18 replaced the photomultiplier tube in *Sigal*. Because the modification proposed by the Examiner will render the binding

assays of *Sigal* unsatisfactory for their intended purpose, there is no suggestion or motivation to make the proposed modification.

3). There is no a reasonable expectation of success by combining *Sigal* with *Meade.*

Although obviousness "does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." M.P.E.P §2143.02 (citation omitted).

Claim 18 recites "a detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety." Because the detector of claim 18 does not detect photons, the ligand binding according to *Sigal* would not be detected. Therefore there is no reasonable expectation of success by combining *Sigal* with *Meade*, and the claimed invention is not obvious.

For the foregoing reasons, there is no suggestion or motivation to for the combination of *Sigal, Meade*, and *Roberts*. Accordingly, the Examiner failed to establish a *prima facie* case of obviousness.

II. The Rejection of Claims 21 Under 35 U.S.C. § 103(a) Over *Sigal* In View of *Meade* And *Roberts*, And Further In View of *Bamdad* Is Improper Because the References In Combination Do Not Teach "An Array of Working Electrodes" And There Is No Motivation to Combine *Sigal* With *Meade* Or *Roberts*

Claim 21 stands rejected under 35 U.S.C. § 103(a) over *Sigal* in view of *Meade* and *Roberts*, and further in view of *Bamdad*.

Claim 21 depends from claim 18 which recites "an array of working electrodes." As presented above, *Sigal*, *Meade* and *Roberts* in combination do not teach "an array of working electrodes." There is also no motivation to combine *Sigal* with *Meade* or *Roberts* because the proposed modification would change the principle of operation of *Sigal*, render the assays of *Sigal* unsatisfactory for their intended purpose, and there is no reasonable expectation of success by combining *Sigal* with *Meade*. These defects are not cured by *Bamdad.*

Bamdad is directed toward derivatized surfaces for surface plasmon resonance experiments. *See* col. 1, ll. 11-12. The Examiner cites *Bamdad* only for the disclosure "that a self-assembling monolayer is made by alkyl thiol functional groups (see columns 9 and 10)." *See* page 10 of the Office Action. Thus *Bamdad* does not teach "an array of working electrodes," nor does it provide the motivation to combine the references.

Accordingly, because the references in combination do not teach "an array of working electrodes," and there is no motivation to combine the references, the Examiner failed to establish a *prima facie* case of obviousness.

III. The Rejection of Claims 22 Under 35 U.S.C. § 103(a) Over *Sigal* In View of *Meade* And *Roberts*, And Further In View of *Gerpheide* Is Improper Because *Gerpheide* Explicitly Teaches Away from *Roberts*.

Claim 22 stands rejected under 35 U.S.C. § 103 over *Sigal* in view of *Meade* and *Roberts*, and further in view of *Gerpheide*.

Claim 22 depends from claim 18 which recites "an array of working electrodes." As presented above, *Sigal*, *Meade* and *Roberts* in combination do not teach "an array of working electrodes." There is also no motivation to combine *Sigal* with *Meade* or *Roberts* because the proposed modification would change the principle of operation of *Sigal*, render the assays of *Sigal* unsatisfactory for their intended purpose, and there is no a reasonable expectation of success by combining *Sigal* with *Meade*. These defects are not cured by *Gerpheide*.

Gerpheide is directed to an apparatus and method for a capacitance-based proximity sensor with interference rejection. *See* Abstract. The Examiner cites *Gerpheide* for the disclosure that it teaches "that the substrate of an electrode array is a printed circuit board (see Figure 3b)." Office Action, at page 11. Thus *Gerpheide* does not teach "an array of working electrodes," nor does it provide the motivation to combine the references.

Furthermore, even assuming, *arguendo*, that *Roberts* teaches an array of working electrodes, *Gerpheide* still explicitly teaches away from *Roberts* because *Roberts* teaches that its

device "includes an absorbent material," and in contrast, *Gerpheide* teaches that the electrode array using materials that are not an absorbent material.

It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be led in a direction divergent from the path that was taken by the applicant. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Roberts teaches at col. 5, ll. 32-34, that its device "includes an absorbent material, having a contact portion proximate to one end for contact with and uptake of the test solution." Each of the conductors in *Roberts* "comprises a plurality of fingers disposed on the absorbent material." *Id.* at lines 37-38. Absorbent material means

> a porous material having a pore size of from 0.05 μm to 50 μm, preferably from 0.45 μm to 5 μm, which is susceptible to traversal by an aqueous medium in response to capillary force. Such materials may be natural polymeric materials, particularly cellulosic materials, such as fiber-containing papers, . . . [and] synthetic or modified naturally occurring polymers, such as nitrocellulose. . . . Nitrocellulose is a preferred absorbent material. *Id.* at col. 12, lines 3- 15.

Gerpheide, however, teaches at col. 5, ll. 28-30, that "the electrode array may utilize a flexible printed circuit board, such as a flex circuit, or stampings of sheet metal or metal foil." One of skill in the art would understand that sheet metal and metal foil are not absorbent materials. Furthermore, one of skill in the art would understand that substrates used in flex circuits are preferably not absorptive. *See* Joseph Fjelstad, Flexible Circuit Technology, 43 (3d ed. 2007) (Exhibit A in the response filed on July 23, 2007) ("Moisture absorption is definitely not desirable for any flexible substrate. Moisture can negatively impact both the manufacturing process (by causing delamination, in process or in assembly) and the performance of the finished product (by altering the material's dielectric constant and increasing signal loss.)")

Therefore, *Gerpheide* explicitly teaches away from *Roberts* because *Roberts* teaches that its device "includes an absorbent material," and in contrast, *Gerpheide* teaches that the electrode array may utilize a flexible printed circuit board, such as a flex circuit, or stampings of sheet metal, which are not absorbent materials.

Accordingly, because the references in combination do not teach "an array of working electrodes," and *Gerpheide* explicitly teaches away from *Roberts* thus there is no motivation to combine the references, the Examiner failed to establish a *prima facie* case of obviousness.

IV. The Examiner Erred in Citing *Kayyem* Which Cannot Preclude Patentability of the Presently Claimed Invention Under U.S.C. § 103.

Claims 23 and 25 stands rejected under 35 U.S.C. 103(a) over *Sigal* in view of *Meade* and *Roberts*, and further in view of *Kayyem*.

Both the instant application and the *Kayyem* patent were, at the time the invention of the instant invention was made, owned by Clinical Micro Sensors, Inc, which was acquired by Osmetch Technology Inc., the current assignee, in 2004. The assignment of the *Kayyem* patent is recorded in Reel/Frame 008406/0741, 008757/0001, 010225/0614, and 021924/0376. The instant application is a continuation of U.S. Appl. No. 09/428,155, issued as U.S. Patent No. 6,541,617 (allowed by the same Examiner), the assignment of which is recorded in Reel/Frame 010625/0568 and 021924/0376. Therefore, according to U.S.C. § 103(c)(1), *Kayyem* cannot preclude patentability of the presently claimed invention under U.S.C. § 103. Accordingly, the rejections of claim 23 and 25 are improper and should be reversed.

V. The Rejections of Claims 23 and 25 Under 35 U.S.C. § 103(a) Over *Sigal* In View of *Meade* and *Roberts* Are Improper Because the References In Combination Do Not Teach "An Array of Working Electrodes" And There Is No Motivation to Combine *Sigal* With *Meade* Or *Roberts*.

Claims 23 and 25 stand rejected under 35 U.S.C. 103(a) over *Sigal* in view of *Meade* and *Roberts*.

Claims 23 and 25 depend from claim 18 which recites "an array of working electrodes." As presented above, *Sigal*, *Meade* and *Roberts* in combination do not teach "an array of working electrodes." There is also no motivation to combine *Sigal* with *Meade* or *Roberts* because the proposed modification would change the principle of operation of *Sigal*, render the assays of

Sigal unsatisfactory for their intended purpose, and there is no a reasonable expectation of success by combining *Sigal* with *Meade*.

Accordingly, because the references in combination do not teach "an array of working electrodes," and there is no motivation to combine the references, the Examiner failed to establish a *prima facie* case of obviousness.

RELIEF REQUESTED

The Appellants respectfully request that the rejections of claims 18, 20- 25, and 27 be reversed, and the application be remanded to the Examiner with instruction to issue a Notice of Allowance.

Respectfully submitted,

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CLAIMS APPENDIX

18. A composition comprising:

a) a substrate comprising an array of working electrodes, wherein each electrode comprises a first binding ligand;

b) a plurality of colloids, each comprising:

i) a second binding ligand; and

ii) an electron transfer moiety; and

c) a detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety.

20. The composition of claim 18 wherein said plurality of colloids further comprise a self-assembled monolayer.

21. The composition of claim 20 wherein said self-assembling monolayer comprises an alkyl chain.

22. The composition of claim 18 wherein said substrate is a printed circuit board.

23. The composition according to claim 18 wherein said electrodes are gold.

24. The composition according to claim 18 wherein said electron transfer moiety is a transition metal complex.

25. The composition according to claim 24 wherein said transition metal complex is ferrocene.

27. The composition according to claim 18 wherein said first binding ligand is a first nucleic acid and said second binding ligand is a second nucleic acid.

EVIDENCE APPENDIX

1. Bamdad et al. (U.S. Patent No. 5,620,850) ("Bamdad"), cited in Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

2. Gerpheide et al. (U.S. Patent No. 5,565,658) ("Gerpheide"), cited in Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

3. Joseph Fjelstad, *Flexible Print Circuits*, in Flexible Circuit Technology (3d ed. 2007). Exhibit A in the response filed on July 23, 2007.

4. Kayyem et al. (U.S. Patent No. 6,096,273), cited in Office Action mailed March 10, 2004, Office Action mailed November 2, 2004, Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

5. Meade et al. (U.S. Patent No. 5,770,369), cited in Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

6. Roberts et al. (U.S. Patent No. 5,958,791) cited in Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

7. Sigal et al. (U.S. Patent No. 6,319,670 B1), cited in Office Action mailed March 10, 2004, Office Action mailed November 2, 2004, Final Office Action mailed August 2, 2005, Office Action mailed June 29, 2006, Final Office Action of January 2, 2007, Office Action of September 27, 2007, and Final Office Action of May 28, 2008.

RELATED PROCEEDINGS APPENDIX

None.